Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

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Appendix

Compliance with Results Reporting in ClinicalTrials.gov

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Table S1. Derivation of Analysis Population and Summary of Exclusion Criteria

Exclusion criterion	Number excluded	Number remaining
Studies downloaded from ClinicalTrials.gov (9/27/2013)	–	152,611
Exclude: Overall recruitment status=WITHDRAWN	2462	150,149
Exclude: Primary completion date ≤ 12/2007, or if missing, completion date ≤ 12/2007	27,364	122,785
Exclude: Study type not INTERVENTIONAL	25,155	97,630
Exclude: Phase 0 or Phase I	14,503	83,127
Exclude: No US FDA oversight*, and (only non-US sites or no biological/device/drug/genetic/radiation intervention)†	50,471	32,656
Exclude: Overall recruitment status not COMPLETED or TERMINATED	16,397	16,259
Exclude: Primary completion date ≥ 9/2012, or if missing, completion date ≥ 9/2012	1801	14,458
Exclude: Primary completion and completion dates missing, and verification date ≤ 12/2007	1078	13,380
Exclude: Primary completion and completion dates missing, and verification date ≥ 9/2012	53	13,327
Studies that are highly likely to be Applicable Clinical Trials (ACTs) and completed/terminated before 9/2012	–	13,327

*IND/IDE Protocol is not public information. Oversight authority by United States: FDA used as a surrogate.
†Number of studies remaining at this step are the highly likely ACTs

Appendix Panel S1. Detailed Definitions of Trial Classifications

Trial characteristics included intervention types, phase, funding source, oversight authorities, enrollment characteristics, site locations, trial purpose, and study design descriptors.[1] A single trial might report multiple interventions, but for classification purposes, each trial was categorized according to one intervention using an algorithm that hierarchically assigned trials with a device intervention to "devices," trials with a biological intervention to "biological," and trials with a drug intervention to "drugs." If none of these was specified, the intervention group was classified as "other." Trials included single-phase (phase 2, 3, or 4) studies, combined-phase trials (1/2 or 2/3), and studies without a phase (device trials). Funding sources were classified as industry, NIH, or "other" based on the recorded lead sponsor and/or collaborator for a study.[2] "Lead sponsor" was defined as the organization or person responsible for overseeing the trial and analyzing study data, while "collaborator" was defined as an "…organization other than the sponsor that provides support for a clinical study. This [support] may include funding, design, implementation, data analysis, or reporting." If industry was listed as a lead sponsor or as a collaborator with no NIH lead sponsor or collaborators, the trial was considered "industry-funded." If the NIH was the lead sponsor or was listed as a collaborator with a non-industry lead sponsor, the trial was considered "NIH-funded." If neither lead sponsor nor collaborators were from the NIH or industry, the trial was considered "other-funded." Other funders included academic institutions (or individual faculty at academic institutions), community-based organizations, and other non-NIH federal agencies.

Oversight authority was defined as the national or international health organization with authority over the protocol. If a trial was conducted under an IND/IDE protocol, it was automatically listed as taking place under FDA oversight. However, sponsors could also identify FDA as having oversight in circumstances when an IND/IDE was not relevant. Site locations were examined for each study and studies were grouped according to whether they listed only U.S. sites, only non-U.S. sites, both U.S. and non-U.S. sites, or sites unknown.

A responsible party could delay the 12-month deadline for submitting results through several mechanisms, including the submission of a "certification of initial use" to ClinicalTrials.gov if a medical product studied in the trial is not approved for market at the time of trial completion. In this case, results must be submitted 30 days after the product is approved. A "certification of new use" may be submitted if a sponsor intends to seek FDA approval, clearance, or licensure of new use of an approved medical product. In this case, results may be delayed for up to 2 years, or for 30 days after the FDA determines approval status, issues a complete response letter, or the application is withdrawn.[3] An extension can be requested to delay results reporting for good cause. A list of trials submitting a certification or an extension request to ClinicalTrials.gov, and the date the request was first submitted, were provided by the NLM (personal communication, Tony Tse, 3/10/2014).

References

1. Tasneem A, Aberle L, Ananth H, Chakraborty S, Chiswell K, McCourt BJ, Pietrobon R. The database for aggregate analysis of ClinicalTrials.gov (AACT) and subsequent regrouping by clinical specialty. PLoS One 2012;7:e33677.

2. Califf RM, Zarin DA, Kramer JM, Sherman RE, Aberle LH, Tasneem A. Characteristics of clinical trials registered in ClinicalTrials.gov, 2007-2010. JAMA 2012;307:1838-47.

3. Food and Drug Administration Amendments Act of 2007. (Public Law No. 110-85 § 801;2007).

Table S2. Trial Characteristics of Highly Likely ACTs Completed or Terminated before September 2012

Baseline Characteristics	All trials (N=13,327)	Results reported by 12 months (N=1790)	Results reported (N=5110)
Primary purpose, n/N (%)			
Treatment	10930/12884 (84.8)	1509/1735 (87.0)	4244/4954 (85.7)
Prevention	990/12884 (7.7)	133/1735 (7.7)	393/4954 (7.9)
Diagnostic	350/12884 (2.7)	43/1735 (2.5)	128/4954 (2.6)
Other	614/12884 (4.8)	50/1735 (2.9)	189/4954 (3.8)
Intervention types*, n/N (%)			
Drug	10797/13327 (81.0)	1465/1790 (81.8)	4178/5110 (81.8)
Biological	1188/13327 (8.9)	168/1790 (9.4)	492/5110 (9.6)
Device	1586/13327 (11.9)	198/1790 (11.1)	581/5110 (11.4)
Genetic	87/13327 (0.7)	2/1790 (0.1)	28/5110 (0.5)
Radiation	287/13327 (2.2)	20/1790 (1.1)	86/5110 (1.7)
Intervention group†, n/N (%)			
Drug	10309/13327 (77.4)	1412/1790 (78.9)	3992/5110 (78.1)
Biological	1185/13327 (8.9)	168/1790 (9.4)	492/5110 (9.6)
Device	1586/13327 (11.9)	198/1790 (11.1)	581/5110 (11.4)
Other[&]	247/13327 (1.9)	12/1790 (0.7)	45/5110 (0.9)
Phase, n/N (%)			
Phase 1/Phase 2	867/13327 (6.5)	64/1790 (3.6)	239/5110 (4.7)
Phase 2	4917/13327 (36.9)	466/1790 (26.0)	1634/5110 (32.0)
Phase 2/Phase 3	333/13327 (2.5)	20/1790 (1.1)	105/5110 (2.1)
Phase 3	3117/13327 (23.4)	646/1790 (36.1)	1512/5110 (29.6)
Phase 4	1928/13327 (14.5)	393/1790 (22.0)	919/5110 (18.0)
N/A	2165/13327 (16.2)	201/1790 (11.2)	701/5110 (13.7)
Site locations, n/N (%)			
US only	8997/13327 (67.5)	1041/1790 (58.2)	3429/5110 (67.1)
Non-US only	612/13327 (4.6)	88/1790 (4.9)	203/5110 (4.0)
Both US and non-US	2950/13327 (22.1)	611/1790 (34.1)	1292/5110 (25.3)
Unknown	768/13327 (5.8)	50/1790 (2.8)	186/5110 (3.6)
Oversight authorities, n/N (%)			
US: FDA	8640/13327 (64.8)	1362/1790 (76.1)	3449/5110 (67.5)
US: Non-FDA only	4089/13327 (30.7)	373/1790 (20.8)	1506/5110 (29.5)
No US oversight authority	598/13327 (4.5)	55/1790 (3.1)	155/5110 (3.0)
Funding source‡, n/N (%)			
Industry	8736/13327 (65.6)	1483/1790 (82.8)	3624/5110 (70.9)

Table S2. Trial Characteristics of Highly Likely ACTs Completed or Terminated before September 2012

Baseline Characteristics	All trials (N=13,327)	Results reported by 12 months (N=1790)	Results reported (N=5110)
NIH	1899/13327 (14.2)	153/1790 (8.5)	739/5110 (14.5)
Other	2692/13327 (20.2)	154/1790 (8.6)	747/5110 (14.6)
Enrollment (no. of trials with data)			
Number of trials	13134	1790	5110
Project Enrollment (Mean ± SD)	294 ± 1550	429 ±1553	374 ± 1567
Overall recruitment status, n/N (%)			
Completed	11128/13327 (83.5)	1521/1790 (85.0)	4286/5110 (83.9)
Terminated	2199/13327 (16.5)	269/1790 (15.0)	824/5110 (16.1)
Primary completion year§, n/N (%)			
2008	3142/13327 (23.6)	370/1790 (20.7)	1372/5110 (26.8)
2009	3051/13327 (22.9)	373/1790 (20.8)	1407/5110 (27.5)
2010	2853/13327 (21.4)	403/1790 (22.5)	1154/5110 (22.6)
2011	2686/13327 (20.2)	418/1790 (23.4)	888/5110 (17.4)
2012	1595/13327 (12.0)	226/1790 (12.6)	289/5110 (5.7)
Number of arms, n/N (%)			
One	4043/12725 (31.8)	474/1757 (27.0)	1457/5066 (28.8)
Two	5611/12725 (44.1)	921/1757 (52.4)	2459/5066 (48.5)
Three or more	3071/12725 (24.1)	362/1757 (20.6)	1150/5066 (22.7)
Randomized allocation¶, n/N (%)	8089/8665 (93.4)	1207/1279 (94.4)	3371/3603 (93.6)
Masking¶, n/N (%)			
Open	1844/8072 (22.8)	324/1207 (26.8)	822/3369 (24.4)
Single-blind	668/8072 (8.3)	79/1207 (6.5)	273/3369 (8.1)
Double-blind	5560/8072 (68.9)	804/1207 (66.6)	2274/3369 (67.5)
Data monitoring committee, n/N (%)			
No	6200/13327 (46.5)	962/1790 (53.7)	2662/5110 (52.1)
Yes	4423/13327 (33.2)	468/1790 (26.1)	1591/5110 (31.1)
Unknown	2704/13327 (20.3)	360/1790 (20.1)	857/5110 (16.8)

*Study may have more than one intervention type and be counted in >1 row.
†Mutually exclusive intervention groups defined as follows: If study has device intervention then classified under device. Otherwise if study has biological intervention then classified under biological. Otherwise if study has drug intervention then classified under Drug. Otherwise classified under other. ‡Funding source derived from lead sponsor and collaborator information. §Study completion year used when primary completion year is missing. If study completion year is also missing, verification year is used. ¶Among studies with >1 arm.
&Other includes radiation and genetic trials.

Table S3. Summary of Results Reporting at ClinicalTrials.gov Stratified by Type of Study
Population: All interventional clinical trials that are completed/terminated prior to September 2012.

	All trials (N=63,375)	HLACTs compl/term >2007 (n=13,327)	Other trials compl/term >2007 (n=25,646)	Trials like ACTs compl/term ≤2007 (n=12,366)	Other trials compl/term ≤2007 (n=12,036)
Results reported by 9/2013, n (% *)	8916 (14.1)	5110 (38.3)	2473 (9.6)	751 (6.1)	582 (4.8)
Results reported within 12 months of primary completion†, n (%)	3185 (5.0)	1790 (13.4)	1287 (5.0)	69 (0.6)	39 (0.3)
Months until results reported for studies with results‡					
n	8890	5097	2460	751	582
Mean ± SD	25.1 ± 19.3	21.8 ± 12.4	18.3 ± 11.6	49.2 ± 30.3	52.7 ± 27.8
Median (IQR)	18 (13- 32)	17 (13- 29)	13 (12- 22)	44 (27- 64)	51 (32- 70)

*Crude percentage, ignoring differing lengths of time from primary completion until database download in September 2013.
†Includes trials that report results within 12 months after the primary completion date.
‡Calculated from primary completion date and date results first posted at ClinicalTrials.gov. If primary completion date is missing then verification date is used. Calculation is rounded up to integer months.

Table S4. Reporting of Study Results Components

Results component	Results reported (N=5110)
Participant flow, n (%)	
Started milestone	5110 (100.0)
Completed milestone	5110 (100.0)
Baseline characteristics, n (%)	
Any baseline results	5110 (100.0)
Number of participants	5110 (100.0)
Age	5103 (99.9)
Sex	5103 (99.9)
Any race or ethnicity	974 (19.1)
Outcome measures, n (%)	
At least one primary outcome	5110 (100.0)
At least one secondary outcome	3677 (72.0)
Adverse events (AEs), n (%)	
No events reported	893 (17.5)
Only serious AEs	244 (4.8)
Only non-serious AEs	891 (17.4)
Serious and non-serious AEs	3082 (60.3)

Table S5. Summary of Results Reporting at ClinicalTrials.gov Stratified by Phase
Population: Highly likely Applicable Clinical Trials that are completed/terminated prior to September 2012.

	All trials (N=13,327)	**Phase1/2 (n=867)**	**Phase 2 (n=4917)**	**Phase 2/3 (n=333)**	**Phase 3 (n=3117)**	**Phase 4 (n=1928)**	**Phase NA (n=2165)**
Results reported by 9/2013, n (%*)	5110 (38.3)	239 (27.6)	1634 (33.2)	105 (31.5)	1512 (48.5)	919 (47.7)	701 (32.4)
Results reported within 12 months of primary completion+, n (%)	1790 (13.4)	64 (7.4)	466 (9.5)	20 (6.0)	646 (20.8)	393 (20.4)	201 (9.3)
For studies with results:							
Months until results reported**							
n	5097	238	1630	105	1504	919	701
Mean ± SD	21.8 ± 12.4	21.9 ± 12.2	24.1 ± 13.6	24.2 ± 13.2	20.2 ± 11.1	20.4 ± 12.0	21.1 ± 12.0
Median (25^{th}-75^{th} percentile)	17 (13-29)	19 (13-29)	20 (13-33)	21 (14-33)	16 (13-25)	16 (13-26)	18 (13-27)
Certification of Delay by 9/2013, n (%)	2100 (15.8)	123 (14.2)	1063 (21.6)	54 (16.2)	790 (25.3)	37 (1.9)	33 (1.5)
For studies with delayed results:							
Results reported by 9/2013, n/N (%)	482/2100 (23.0)	9/123 (7.3)	149/1063 (14.0)	14/54 (25.9)	289/790 (36.6)	13/37 (35.1)	8/33 (24.2)
Months until results reported**							
n	482	9	149	14	289	13	8
Mean ± SD	28.7 ± 11.9	27.1 ± 9.3	33.5 ± 13.2	35.4 ± 13.4	26.3 ± 10.4	19.7 ± 9.5	29.1 ± 11.4
Median (25th-75^{th} percentile)	26 (19-36)	25 (20-35)	34 (22-43)	34 (23-48)	24 (19-32)	18 (16-20)	27 (20-38)
For studies without delayed results:							
Results reported by 9/2013, n/N (%)	4628/11227 (41.2)	230/744 (30.9)	1485/3854 (38.5)	91/279 (32.6)	1223/2327 (52.6)	906/1891 (47.9)	693/2132 (32.5)
Months until results reported**							
n	4615	229	1481	91	1215	906	693
Mean ± SD	21.1 ± 12.3	21.7 ± 12.3	23.1 ± 13.3	22.5 ± 12.3	18.8 ± 10.8	20.4 ± 12.1	21.0 ± 12.0
Median (25^{th}-75^{th} percentile)	16 (13-27)	19 (13-28)	19 (13-31)	18 (14-30)	13 (13-23)	15 (13-26)	17 (13-27)
Results reported/delayed by 9/2013, n (%)							
No results, no delay	6599 (49.5)	514 (59.3)	2369 (48.2)	188 (56.5)	1104 (35.4)	985 (51.1)	1439 (66.5)

Table S5. Summary of Results Reporting at ClinicalTrials.gov Stratified by Phase
Population: Highly likely Applicable Clinical Trials that are completed/terminated prior to September 2012.

	All trials (N=13,327)	Phase1/2 (n=867)	Phase 2 (n=4917)	Phase 2/3 (n=333)	Phase 3 (n=3117)	Phase 4 (n=1928)	Phase NA (n=2165)
No results, delay	1618 (12.1)	114 (13.1)	914 (18.6)	40 (12.0)	501 (16.1)	24 (1.2)	25 (1.2)
Results++	5110 (38.3)	239 (27.6)	1634 (33.2)	105 (31.5)	1512 (48.5)	919 (47.7)	701 (32.4)
Results reported/delayed within 12 months of primary completion, n (%)							
No results, no delay	10706 (80.4)	769 (88.8)	4062 (82.7)	295 (88.6)	2108 (67.8)	1517 (78.7)	1955 (90.3)
No results, delay	818 (6.1)	33 (3.8)	385 (7.8)	18 (5.4)	355 (11.4)	18 (0.9)	9 (0.4)
Results++	1790 (13.4)	64 (7.4)	466 (9.5)	20 (6.0)	646 (20.8)	393 (20.4)	201 (9.3)

* Crude percentage, ignoring differing lengths of time from primary completion until database download in September 2013.
\+ Includes trials that report results within 12 months after the primary completion date.
** Calculated from primary completion date and date results first posted at ClinicalTrials.gov. If primary completion date is missing then verification date is used. Calculation is rounded up to integer months.
++ Includes trials reporting results that also report a delay in results reporting.

Table S6. Summary of Results Reporting by Trial Characteristics
Population: Highly Likely ACTs Completed/Terminated prior to September 2012

Characteristic	Results reported by 9/2013 n/N (%)	Results reported within 12 months* n/N (%)	Certification/extension request by 9/2013 n/N (%)
Primary purpose			
Treatment	4244/10930 (38.8)	1509/10920 (13.8)	1845/10930 (16.9)
Prevention	393/990 (39.7)	133/989 (13.4)	172/990 (17.4)
Diagnostic	128/350 (36.6)	43/349 (12.3)	17/350 (4.9)
Other	189/614 (30.8)	50/613 (8.2)	37/614 (6.0)
Intervention group†			
Device	581/1586 (36.6)	198/1586 (12.5)	67/1586 (4.2)
Biological	492/1185 (41.5)	168/1183 (14.2)	275/1185 (23.2)
Drug	3992/10309 (38.7)	1412/10298 (13.7)	1756/10309 (17.0)
Other	45/247 (18.2)	12/247 (4.9)	2/247 (0.8)
Phase			
Phase 1/Phase 2	239/867 (27.6)	64/866 (7.4)	123/867 (14.2)
Phase 2	1634/4917 (33.2)	466/4913 (9.5)	1063/4917 (21.6)
Phase 2/Phase 3	105/333 (31.5)	20/333 (6.0)	54/333 (16.2)
Phase 3	1512/3117 (48.5)	646/3109 (20.8)	790/3117 (25.3)
Phase 4	919/1928 (47.7)	393/1928 (20.4)	37/1928 (1.9)
N/A	701/2165 (32.4)	201/2165 (9.3)	33/2165 (1.5)
Site locations			
US only	3429/8997 (38.1)	1041/8991 (11.6)	1019/8997 (11.3)
Non-US only	203/612 (33.2)	88/612 (14.4)	149/612 (24.3)

Table S6. Summary of Results Reporting by Trial Characteristics
Population: Highly Likely ACTs Completed/Terminated prior to September 2012

Characteristic	Results reported by 9/2013 n/N (%)	Results reported within 12 months* n/N (%)	Certification/extension request by 9/2013 n/N (%)
Both US and non-US	1292/2950 (43.8)	611/2944 (20.8)	902/2950 (30.6)
Unknown	186/768 (24.2)	50/767 (6.5)	30/768 (3.9)
Oversight authorities			
US: FDA	3449/8640 (39.9)	1362/8630 (15.8)	2052/8640 (23.8)
US: Non-FDA only	1506/4089 (36.8)	373/4086 (9.1)	34/4089 (0.8)
No US oversight authority	155/598 (25.9)	55/598 (9.2)	14/598 (2.3)
Funding source‡			
Industry	3624/8736 (41.5)	1483/8728 (17.0)	2015/8736 (23.1)
NIH	739/1899 (38.9)	153/1895 (8.1)	51/1899 (2.7)
Other	747/2692 (27.7)	154/2691 (5.7)	34/2692 (1.3)
Enrollment (from registration data)			
0	3/20 (15.0)	2/20 (10.0)	1/20 (5.0)
1-10	426/1151 (37.0)	115/1151 (10.0)	66/1151 (5.7)
11-50	1470/4237 (34.7)	404/4236 (9.5)	366/4237 (8.6)
51-100	804/2307 (34.9)	275/2305 (11.9)	321/2307 (13.9)
101-500	1592/3852 (41.3)	655/3845 (17.0)	899/3852 (23.3)
501-1000	481/971 (49.5)	216/970 (22.3)	291/971 (30.0)
1001-2000	207/369 (56.1)	75/367 (20.4)	95/369 (25.7)
2001-5000	84/154 (54.5)	28/154 (18.2)	47/154 (30.5)

Table S6. Summary of Results Reporting by Trial Characteristics
Population: Highly Likely ACTs Completed/Terminated prior to September 2012

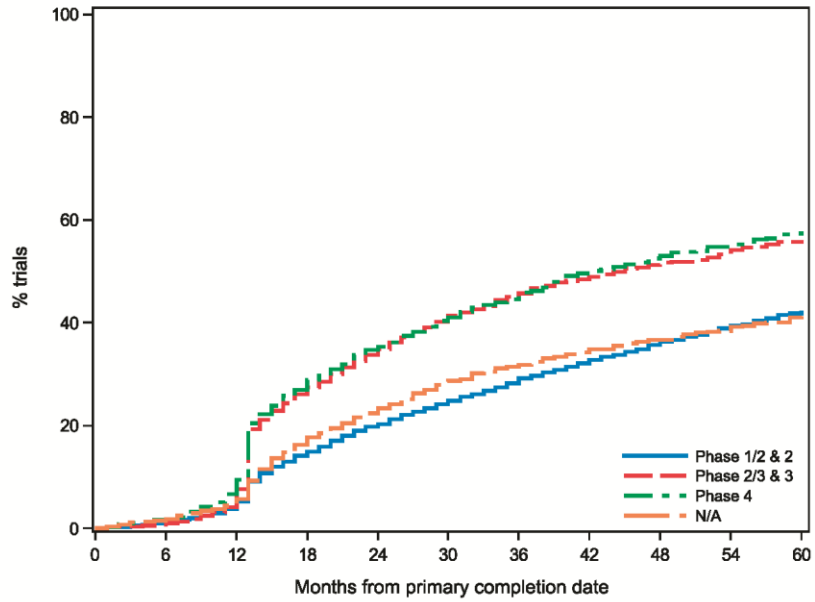
Characteristic	Results reported by 9/2013 n/N (%)	Results reported within 12 months* n/N (%)	Certification/extension request by 9/2013 n/N (%)
> 5000	43/73 (58.9)	20/73 (27.4)	13/73 (17.8)
Overall recruitment status			
Completed	4286/11128 (38.5)	1521/11116 (13.7)	1838/11128 (16.5)
Terminated	824/2199 (37.5)	269/2198 (12.2)	262/2199 (11.9)
Primary completion year§			
2008	1372/3142 (43.7)	370/3142 (11.8)	466/3142 (14.8)
2009	1407/3051 (46.1)	373/3051 (12.2)	477/3051 (15.6)
2010	1154/2853 (40.4)	403/2848 (14.2)	453/2853 (15.9)
2011	888/2686 (33.1)	418/2684 (15.6)	479/2686 (17.8)
2012	289/1595 (18.1)	226/1589 (14.2)	225/1595 (14.1)
Months to primary completion¶			
<6 months	582/1386 (42.0)	213/1386 (15.4)	298/1386 (21.5)
6-12 months	744/2032 (36.6)	261/2032 (12.8)	478/2032 (23.5)
12-18 months	728/1825 (39.9)	264/1825 (14.5)	383/1825 (21.0)
18-24 months	636/1686 (37.7)	232/1686 (13.8)	347/1686 (20.6)
24-36 months	917/2312 (39.7)	314/2312 (13.6)	317/2312 (13.7)
36-48 months	557/1473 (37.8)	191/1471 (13.0)	148/1473 (10.0)
≥48 months	942/2518 (37.4)	311/2507 (12.4)	129/2518 (5.1)
Number of arms			
One	1457/4043 (36.0)	474/4041 (11.7)	339/4043 (8.4)

Table S6. Summary of Results Reporting by Trial Characteristics
Population: Highly Likely ACTs Completed/Terminated prior to September 2012

Characteristic	Results reported by 9/2013 n/N (%)	Results reported within 12 months* n/N (%)	Certification/extension request by 9/2013 n/N (%)
Two	2459/5611 (43.8)	921/5604 (16.4)	836/5611 (14.9)
Three or more	1150/3071 (37.4)	362/3069 (11.8)	912/3071 (29.7)
Randomized allocation (studies with >1 arm)			
No	232/576 (40.3)	72/576 (12.5)	84/576 (14.6)
Yes	3371/8089 (41.7)	1207/8080 (14.9)	1664/8089 (20.6)
Masking (randomized studies with >1 arm)			
Open	822/1844 (44.6)	324/1840 (17.6)	235/1844 (12.7)
Single-blind	273/668 (40.9)	79/668 (11.8)	68/668 (10.2)
Double-blind	2274/5560 (40.9)	804/5555 (14.5)	1361/5560 (24.5)
Data monitoring committee			
No	2662/6200 (42.9)	962/6198 (15.5)	1113/6200 (18.0)
Yes	1591/4423 (36.0)	468/4417 (10.6)	619/4423 (14.0)
Unknown	857/2704 (31.7)	360/2699 (13.3)	368/2704 (13.6)

*Includes trials that reported results within 12 months after the primary completion date.
†Mutually exclusive intervention groups defined as follows. If study has device intervention then classified under device. Otherwise if study has biological intervention then classified under biological. Otherwise if study has drug intervention then classified under Drug. Otherwise classified under other.
‡Funding source derived from lead sponsor and collaborator information.
§Study completion year used when primary completion year is missing. If study completion year also missing, verification year is used.
¶Study duration computed from study start date and primary completion date. Completion date used
if primary completion date is missing. Verification date used if completion date is also missing.

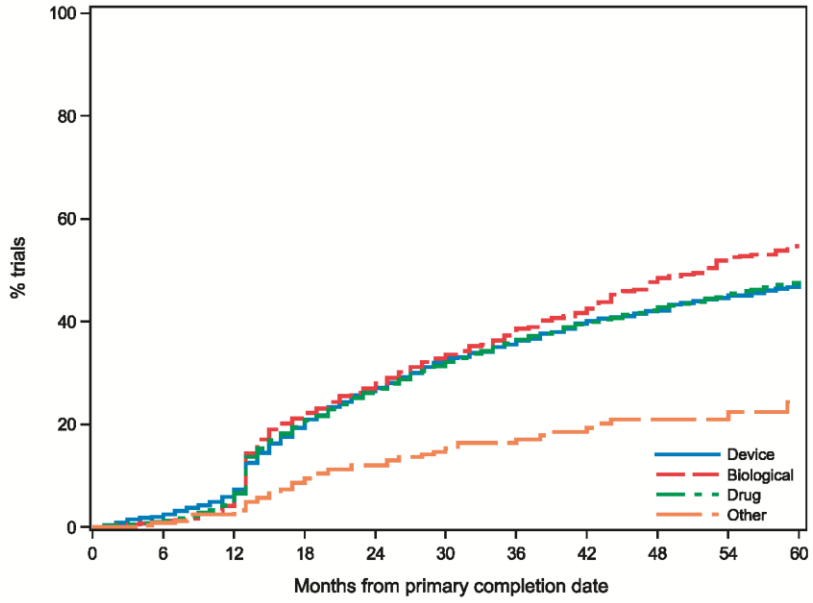
Figure S1. Cumulative Percentage of Trials Reporting Results versus Months from Primary Completion Date Stratified by Phase



Number of trials in cohort

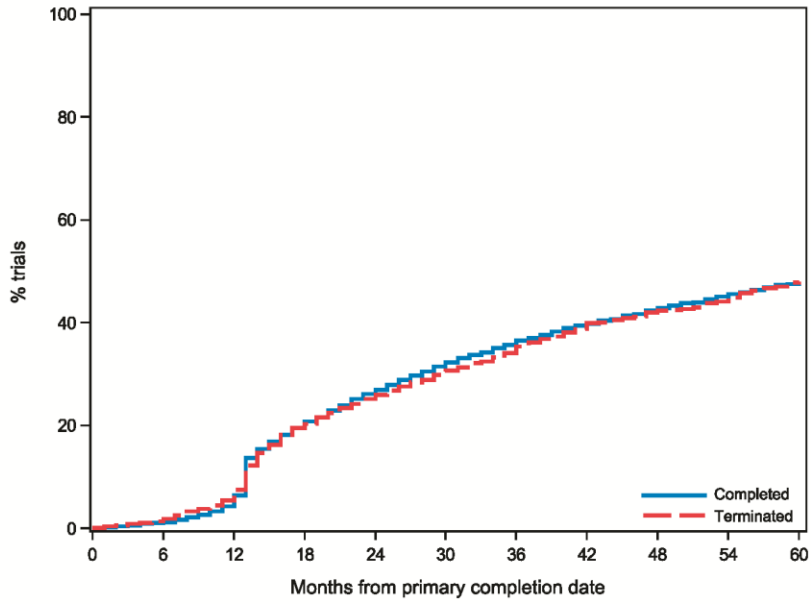
Phase	0 months	<12 months	<24 months	<36 months	<48 months	<60 months
Phase 1/2 & 2	5779	5563	3973	2730	1662	692
Phase 2/3 & 3	3442	3300	1918	1214	777	330
Phase 4	1928	1801	1059	685	407	185
N/A	2165	2070	1377	912	542	239

Figure S2. Cumulative Percentage of Trials Reporting Results versus Months from Primary Completion Date Stratified by Intervention Type



Number of trials in cohort						
Intervention	0 months	<12 months	<24 months	<36 months	<48 months	<60 months
Device	1586	1494	925	589	332	138
Biological	1183	1134	730	455	234	99
Drug	10298	9865	6489	4371	2747	1174
Other	247	241	183	126	75	35

Figure S3. Cumulative Percentage of Trials Reporting Results versus Months from Primary Completion Date Stratified by Terminated/Completed



Number of trials in cohort

Status	0 months	<12 months	<24 months	<36 months	<48 months	<60 months
Completed	11116	10654	6934	4636	2836	1234
Terminated	2198	2080	1393	905	552	212

Table S7. Results Reporting within 12 Months and through 60 Months of Primary Completion Date for Highly Likely ACTs Completed or Terminated before September 2012

	Results reporting within 12 months*		Results reporting through 60 months†	
Baseline trial characteristics	**Multivariable OR**	**95% CI**	**Multivariable HR**	**95% CI**
Primary purpose vs treatment				
Prevention	0.86	(0.70- 1.07)	0.91	(0.81 - 1.01)
Diagnostic	0.93	(0.66 - 1.31)	1.05	(0.87 - 1.25)
Other	0.73	(0.53 – 0.99)	0.84	(0.72 - 0.97)
Intervention group vs drug				
Device	0.88	(0.72 - 1.07)	0.95	(0.86 - 1.06)
Biological	1.16	(0.95 - 1.44)	1.17	(1.06 - 1.30)
Other	0.48	(0.26 - 0.90)	0.53	(0.39 - 0.71)
Phase vs. phase 4				
Phase 1/Phase 2	0.28	(0.21 - 0.38)	0.46	(0.40 - 0.54)
Phase 2	0.33	(0.27 - 0.39)	0.54	(0.49- 0.59)
Phase 2/Phase 3	0.22	(0.14 - 0.36)	0.54	(0.44 - 0.66)
Phase 3	0.60	(0.50 - 0.70)	0.80	(0.72 - 0.88)
N/A	0.56	(0.45 - 0.70)	0.71	(0.63 - 0.79)
No US FDA oversight vs. US FDA oversight	0.61	(0.52 - 0.71)	0.86	(0.80 - 0.93)
Funding source vs. NIH				
Industry	1.62	(1.34 - 1.97)	0.97	(0.89 -1.07)
Other	0.58	(0.45 - 0.75)	0.62	(0.56 - 0.70)
Total enrollment‡ through 1000 participants				

Table S7. Results Reporting within 12 Months and through 60 Months of Primary Completion Date for Highly Likely ACTs Completed or Terminated before September 2012

	Results reporting within 12 months*		Results reporting through 60 months†	
Baseline trial characteristics	**Multivariable OR**	**95% CI**	**Multivariable HR**	**95% CI**
Per doubling < 32 participants	0.96	(0.88 - 1.04)	0.90	(0.86 - 0.93)
Per doubling >32 participants	1.12	(1.07 - 1.17)	1.08	(1.06 - 1.11)
Terminated vs. completed	0.97	(0.83 - 1.11)	0.94	(0.86 - 1.02)
Primary completion year				
Per year increase <2010	1.21	(1.12 - 1.31)	1.18	(1.13 - 1.22)
Per year increase >2010	1.01	(0.93 - 1.11)	0.94	(0.88 - 0.99)
Study duration through 24 months				
Per 3 months increase <12 months	0.89	(0.83 – 0.96)	0.94	(0.89 - 0.97)
Per 3 months increase >12 months	1.07	(1.03 - 1.11)	1.05	(1.03 - 1.07)
Number of arms vs. one				
Two	1.09	(0.82 - 1.45)	1.31	(1.13 - 1.51)
Three or more	0.71	(0.52 - 0.96)	1.02	(0.88 - 1.19)
Use of randomized allocation§	1.26	(0.96 - 1.69)	0.97	(0.83 - 1.13)
Masking vs. open-label§				
Single-blind	0.65	(0.49 - 0.87)	0.96	(0.83 - 1.10)
Double-blind	0.73	(0.63 - 0.85)	0.88	(0.81 - 0.96)

*Logistic regression model
†Cox regression model
‡Enrollment from registration data.
§One-arm studies assigned a value of “no” for randomization. Nonrandomized studies assigned a value of “open” for blinding.

Additional Regression Analyses

To evaluate the effect of accounting for trials with known exceptions to reporting requirements, we conducted two alternative logistic regression analyses: the first excluding trials submitting a certification/extension request within 12 months of completion; the second excluding trials submitting a request at any time through 9/27/2013. We also conducted several alternative Cox regression analyses: in the first, trials submitting a certification/extension request at any time through 9/27/2013 were excluded; in the second, a time-dependent covariate was included to indicate whether reporting requirements were in effect. This indicator was set to "no" during the initial period after completion, and then switched to "yes" at 12 months for trials without a certification/extension request; for trials with a request, the indicator was switched to "yes" at 12 months after completion, or at 24 months after certification/extension submission, whichever was later. Because the true date that trials with a certification/extension requests were required to report was unknown, we repeated analyses using 18, 12, and 0 months.

Results of these analyses are presented in Tables S8 through S14 below.

Table S8. Sensitivity Analysis

Multivariable logistic regression model for results reporting within 12 months after primary completion date. This analysis excludes studies with a certification or extension request ≤ 12 months from primary completion date.

Characteristic	Multivariable OR	95% CI	P Value
Primary purpose vs. treatment			0.149
Prevention	0.87	(0.70 - 1.08)	
Diagnostic	0.92	(0.65 - 1.30)	
Other	0.73	(0.53 - 1.00)	
Intervention group vs. drug			0.003
Device	0.85	(0.69 - 1.04)	
Biological	1.25	(1.03 - 1.52)	
Other	0.46	(0.24 - 0.86)	
Phase vs. phase 4			<0.001
Phase 1/phase 2	0.29	(0.21 - 0.39)	
Phase 2	0.36	(0.30 - 0.42)	
Phase 2/phase 3	0.23	(0.14 - 0.37)	
Phase 3	0.67	(0.56 - 0.80)	
N/A	0.58	(0.46 - 0.71)	
No US FDA oversight vs. US FDA oversight	0.58	(0.50 - 0.67)	<0.001
Funding source vs. NIH			<0.001
Industry	1.77	(1.46 – 2.15)	
Other	0.61	(0.47 - 0.78)	
Total enrollment*, through 1000 participants			<0.001
Per doubling <32 participants	0.95	(0.88 - 1.04)	
Per doubling >32 participants	1.14	(1.09 - 1.19)	
Terminated vs. completed	0.92	(0.79 - 1.09)	0.337
Primary completion year			<0.001
Per year increase <2010	1.26	(1.17 - 1.37)	
Per year increase >2010	1.05	(0.96 - 1.14)	
Study duration, through 24 months			0.002
Per 3 months increase <12 months	0.88	(0.82-0.95)	

Table S8. Sensitivity Analysis

Multivariable logistic regression model for results reporting within 12 months after primary completion date. This analysis excludes studies with a certification or extension request ≤ 12 months from primary completion date.

Characteristic	Multivariable OR	95% CI	P Value
Per 3 months increase >12 months	1.06	(1.02-1.11)	
Number of arms vs. one			<0.001
Two	1.12	(0.84 - 1.49)	
Three or more	0.73	(0.53 – 0.99)	
Use of randomized allocation†	1.25	(0.92 - 1.69)	0.148
Masking vs. open-label†			<0.001
Single-blind	0.66	(0.49 - 0.89)	
Double-blind	0.73	(0.62 - 0.86)	

*Enrollment from registration data.

†Single-arm studies assigned a value of “no” for randomization. Non-randomized studies assigned a value of “open” for blinding.

Regression model fit in 11,423 studies with non-missing covariates. 1677 (14.7%) of these studies reported results within 12 months after primary completion date.

Table S9. Sensitivity Analysis

Multivariable logistic regression model for results reporting within 12 months after primary completion date. Excludes studies with a certification or extension request received at any time at or before September 2013.

Characteristic	Multivariable OR	95% CI	P Value
Primary purpose vs. treatment			0.103
Prevention	0.83	(0.66 - 1.03)	
Diagnostic	0.88	(0.62 - 1.25)	
Other	0.74	(0.54 - 1.02)	
Intervention group vs. drug			<0.001
Device	0.84	(0.68 - 1.03)	
Biological	1.32	(1.08 - 1.62)	
Other	0.42	(0.22 - 0.78)	
Phase vs. phase 4			<0.001
Phase 1/phase 2	0.34	(0.25 - 0.47)	
Phase 2	0.44	(0.37 - 0.52)	
Phase 2/phase 3	0.27	(0.17 - 0.45)	
Phase 3	0.80	(0.67 - 0.95)	
N/A	0.61	(0.49 - 0.76)	
No US FDA oversight vs. US FDA oversight	0.53	(0.46 - 0.62)	<0.001
Funding source vs. NIH			<0.001
Industry	2.06	(1.70 – 2.15)	
Other	0.66	(0.51 - 0.85)	
Total enrollment*, through 1000 participants			<0.001
Per doubling <32 participants	0.96	(0.88 - 1.04)	
Per doubling >32 participants	1.16	(1.11 - 1.22)	
Terminated vs. completed	0.92	(0.78 - 1.09)	0.34
Primary completion year			<0.001
Per year increase <2010	1.30	(1.19 - 1.41)	
Per year increase >2010	1.00	(0.92 - 1.10)	
Study duration, through 24 months			0.01
Per 3 months increase <12 months	0.89	(0.83-0.96)	
Per 3 months increase >12 months	1.03	(0.99-1.08)	

Table S9. Sensitivity Analysis

Multivariable logistic regression model for results reporting within 12 months after primary completion date. Excludes studies with a certification or extension request received at any time at or before September 2013.

Characteristic	Multivariable OR	95% CI	P Value
Number of arms vs. one			<0.001
Two	1.14	(0.85 - 1.53)	
Three or more	0.79	(0.58 – 1.08)	
Use of randomized allocation†	1.25	(0.92 - 1.69)	0.156
Masking vs. open-label†			0.002
Single-blind	0.67	(0.50 - 0.90)	
Double-blind	0.77	(0.65 - 0.90)	

*Enrollment from registration data.

†Single-arm studies assigned a value of "no" for randomization. Non-randomized studies assigned a value of "open" for blinding.

Regression model fit in 10,189 studies with non-missing covariates. 1677 (16.5%) of these studies reported results within 12 months after primary completion date.

Table S10. Sensitivity Analysis: Multivariable Cox Regression Model for Time to Results Reporting Post Primary Completion Date
This analysis excludes studies with a certification or extension request at any time at or before 2013.

Characteristic	Multivariable HR	95% CI	P Value
Primary purpose vs. treatment			0.018
Prevention	0.87	(0.77 - 0.97)	
Diagnostic	0.98	(0.82 - 1.18)	
Other	0.84	(0.72 - 0.98)	
Intervention group vs. drug			<0.001
Device	0.93	(0.84 - 1.04)	
Biological	1.23	(1.11 - 1.38)	
Other	0.48	(0.35- 0.66)	
Phase vs. phase 4			<0.001
Phase 1/phase 2	0.54	(0.46 - 0.63)	
Phase 2	0.65	(0.60 - 0.72)	
Phase 2/phase 3	0.58	(0.46 - 0.72)	
Phase 3	0.86	(0.78 - 0.95)	
N/A	0.74	(0.66 - 0.82)	
No US FDA oversight vs. US FDA oversight	0.79	(0.73 - 0.85)	<0.001
Funding source vs. NIH			<0.001
Industry	1.15	(1.05 - 1.26)	
Other	0.67	(0.60 - 0.75)	
Total enrollment*, through 1000 participants			<0.001
Per doubling < 32 participants	0.90	(0.86 - 0.94)	
Per doubling > 32 participants	1.11	(1.08 - 1.13)	
Terminated vs. completed	0.93	(0.85 - 1.01)	0.096
Primary completion year			<0.001
Per year increase <2010	1.21	(1.16 - 1.26)	
Per year increase >2010	0.93	(0.88 - 0.99)	
Study duration through 24 months			0.002
Per 3 months increase <12 months	0.93	(0.89 - 0.97)	
Per 3 months increase >12 months	1.03	(1.01 - 1.06)	
Number of arms vs. one			<0.001
Two	1.35	(1.16 - 1.57)	
Three or more	1.08	(0.92 - 1.26)	
Use of randomized allocation†	0.98	(0.84 - 1.15)	0.818

Table S10. Sensitivity Analysis: Multivariable Cox Regression Model for Time to Results Reporting Post Primary Completion Date

This analysis excludes studies with a certification or extension request at any time at or before 2013.

Characteristic	Multivariable HR	95% CI	P Value
Masking vs. open-label†			0.14
Single-blind	0.94	(0.81 - 1.09)	
Double-blind	0.92	(0.84 - 1.00)	

*Enrollment from registration data.

†Single-arm studies assigned a value of "no" for randomization. Non-randomized studies assigned a value of "open" for blinding.

Regression model fit in 10,189 studies that had non-missing covariates. Of these studies, 4412 (43.3%) had reported results by 9/27/2013.

Table S11. Sensitivity Analysis, Time-Dependent Covariate Analysis

Multivariable Cox regression model for time to results reporting post primary completion date. Analysis includes a time-dependent variable in the model that indicates whether the results reporting requirement is in effect. This analysis assumes that the certification or extension request expires 24 months after it is submitted.

Characteristic	Multivariable HR	95% CI	P Value
Primary purpose vs. treatment			0.026
Prevention	0.90	(0.80 – 1.00)	
Diagnostic	1.02	(0.83 - 1.22)	
Other	0.83	(0.72 - 0.97)	
Intervention group vs. drug			<0.001
Device	0.94	(0.85 - 1.04)	
Biological	1.22	(1.10 - 1.35)	
Other	0.50	(0.37- 0.67)	
Phase vs. phase 4			<0.001
Phase 1/phase 2	0.49	(0.42 - 0.57)	
Phase 2	0.59	(0.53 - 0.64)	
Phase 2/phase 3	0.57	(0.47 - 0.71)	
Phase 3	0.87	(0.78 - 0.95)	
N/A	0.72	(0.65 - 0.81)	
No US FDA oversight vs. US FDA oversight	0.80	(0.75 - 0.87)	<0.001
Funding source vs. NIH			<0.001
Industry	1.08	(0.99 - 1.18)	
Other	0.65	(0.58 - 0.72)	
Total enrollment*, through 1000 participants			<0.001
Per doubling < 32 participants	0.90	(0.86 - 0.94)	
Per doubling > 32 participants	1.10	(1.07- 1.13)	
Terminated vs. completed	0.92	(0.85 - 1.00)	0.041
Primary completion year			<0.001
Per year increase <2010	1.19	(1.14 - 1.24)	
Per year increase >2010	0.94	(0.89 - 0.99)	
Study duration through 24 months			<0.001
Per 3 months increase <12 months	0.93	(0.89 - 0.97)	
Per 3 months increase >12 months	1.04	(1.01 - 1.06)	
Number of arms vs. one			<0.001

Table S11. Sensitivity Analysis, Time-Dependent Covariate Analysis

Multivariable Cox regression model for time to results reporting post primary completion date. Analysis includes a time-dependent variable in the model that indicates whether the results reporting requirement is in effect. This analysis assumes that the certification or extension request expires 24 months after it is submitted.

Characteristic	Multivariable HR	95% CI	P Value
Two	1.33	(1.15 - 1.53)	
Three or more	1.07	(0.92 - 1.25)	
Use of randomized allocation†	0.97	(0.83 - 1.12)	0.658
Masking vs. open-label†			0.074
Single-blind	0.96	(0.83 - 1.10)	
Double-blind	0.91	(0.83 – 0.99)	
Result reporting requirement in effect	2.65	(2.38- 2.96)	<0.001

*Enrollment from registration data.

†Single-arm studies assigned a value of "no" for randomization. Non-randomized studies assigned a value of "open" for blinding.

Regression model fit in 12247 studies that had non-missing covariates. Of these studies, 4889 (39.9%) had reported results by 9/27/2013.

Table S12. Sensitivity Analysis, Time-Dependent Covariate Analysis

Multivariable Cox regression model for time to results reporting post primary completion date. This analysis includes a time-dependent variable in the model that indicates whether the results reporting requirement is in effect. This analysis assumes that the certification or extension request expires 24 months after it is submitted.

Characteristic	Multivariable HR	95% CI	P Value
Primary purpose vs. treatment			0.026
Prevention	0.90	(0.80 – 1.00)	
Diagnostic	1.02	(0.83 - 1.22)	
Other	0.83	(0.72 - 0.97)	
Intervention group vs. drug			<0.001
Device	0.94	(0.85 - 1.04)	
Biological	1.22	(1.10 - 1.35)	
Other	0.50	(0.37- 0.67)	
Phase vs. phase 4			<0.001
Phase 1/phase 2	0.49	(0.42 - 0.57)	
Phase 2	0.59	(0.53 - 0.64)	
Phase 2/phase 3	0.57	(0.47 - 0.71)	
Phase 3	0.87	(0.78 - 0.95)	
N/A	0.72	(0.65 - 0.81)	
No US FDA oversight vs. US FDA oversight	0.80	(0.75 - 0.87)	<0.001
Funding source vs. NIH			<0.001
Industry	1.08	(0.99 - 1.18)	
Other	0.65	(0.58 - 0.72)	
Total enrollment*, through 1000 participants			<0.001
Per doubling < 32 participants	0.90	(0.86 - 0.94)	
Per doubling > 32 participants	1.10	(1.07- 1.13)	
Terminated vs. completed	0.92	(0.85 - 1.00)	0.041
Primary completion year			<0.001
Per year increase <2010	1.19	(1.14 - 1.24)	
Per year increase >2010	0.94	(0.89 - 0.99)	
Study duration through 24 months			<0.001
Per 3 months increase <12 months	0.93	(0.89 - 0.97)	
Per 3 months increase >12 months	1.04	(1.01 - 1.06)	
Number of arms vs. one			<0.001

Table S12. Sensitivity Analysis, Time-Dependent Covariate Analysis

Multivariable Cox regression model for time to results reporting post primary completion date. This analysis includes a time-dependent variable in the model that indicates whether the results reporting requirement is in effect. This analysis assumes that the certification or extension request expires 24 months after it is submitted.

Characteristic	Multivariable HR	95% CI	P Value
Two	1.33	(1.15 - 1.53)	
Three or more	1.07	(0.92 - 1.25)	
Use of randomized allocation†	0.97	(0.83 - 1.12)	0.658
Masking vs. open-label†			0.074
Single-blind	0.96	(0.83 - 1.10)	
Double-blind	0.91	(0.83 – 0.99)	
Result reporting requirement in effect	2.65	(2.38- 2.96)	<0.001

*Enrollment from registration data.

†Single-arm studies assigned a value of "no" for randomization. Non-randomized studies assigned a value of "open" for blinding.

Regression model fit in 12,247 studies that had non-missing covariates. Of these studies, 4889 (39.9%) had reported results by 9/27/2013.

Table S13. Sensitivity Analyses of Time-Dependent Covariate Analysis

	Assume certification/ extension expires at 18 months		Assume certification/ extension expires at 12 months		Assume certification/ extension expires at 0 months	
Characteristic	**Multivariable HR**	**95% CI**	**Multivariable HR**	**95% CI**	**Multivariable HR**	**95% CI**
Primary purpose, vs. Treatment						
Prevention	0.89	(0.80 - 1.00)	0.89	(0.80 - 0.99)	0.89	(0.80 - 1.00)
Diagnostic	1.02	(0.85 - 1.22)	1.02	(0.85 - 1.22)	1.03	(0.86 - 1.24)
Other	0.83	(0.72 - 0.97)	0.83	(0.72 - 0.97)	0.83	(0.72 - 0.97)
Intervention group, vs. Drug						
Device	0.94	(0.85 - 1.04)	0.94	(0.85 - 1.05)	0.96	(0.86 - 1.06)
Biological	1.21	(1.10 - 1.34)	1.20	(1.09 - 1.33)	1.18	(1.06 - 1.30)
Other	0.50	(0.37 - 0.68)	0.50	(0.37 - 0.68)	0.51	(0.38 - 0.69)
Phase, vs. Phase 4						
Phase 1/Phase 2	0.49	(0.42 - 0.57)	0.49	(0.42 - 0.58)	0.49	(0.42 - 0.58)
Phase 2	0.58	(0.53 - 0.64)	0.58	(0.53 - 0.64)	0.57	(0.52 - 0.63)
Phase 2/Phase 3	0.57	(0.47 - 0.70)	0.57	(0.47 - 0.71)	0.57	(0.47 - 0.71)
Phase 3	0.86	(0.78 - 0.95)	0.86	(0.78 - 0.95)	0.84	(0.76 - 0.92)
N/A	0.72	(0.65 - 0.81)	0.72	(0.65 - 0.81)	0.72	(0.65 - 0.80)
No FDA oversight, vs. FDA oversight	0.81	(0.75 - 0.87)	0.81	(0.75 - 0.87)	0.83	(0.77 - 0.89)
Funding source, vs. NIH						
Industry	1.07	(0.98 - 1.17)	1.07	(0.98 - 1.17)	1.04	(0.95 - 1.14)
Other	0.65	(0.58 - 0.72)	0.65	(0.58 - 0.72)	0.64	(0.57 - 0.72)
Total enrollment* through 1000 participants						
Per doubling < 32 participants	0.90	(0.86 - 0.93)	0.90	(0.86 - 0.93)	0.90	(0.86 - 0.93)
Per doubling > 32 participants	1.10	(1.07 - 1.12)	1.10	(1.07 - 1.12)	1.09	(1.06 - 1.11)
Terminated, vs. Completed	0.92	(0.85 - 1.00)	0.92	(0.85 - 1.00)	0.94	(0.86 - 1.02)
Primary completion year						
Per year increase <2010	1.19	(1.14 - 1.24)	1.18	(1.13 - 1.23)	1.16	(1.11 - 1.20)
Per year increase >2010	0.94	(0.89 - 0.99)	0.94	(0.88 - 0.99)	0.92	(0.87 - 0.97)
Study duration, through 24 months						
Per 3 months increase <12 months	0.93	(0.89 - 0.97)	0.93	(0.89 - 0.97)	0.93	(0.89 - 0.97)

Table S13. Sensitivity Analyses of Time-Dependent Covariate Analysis

	Assume certification/ extension expires at 18 months		Assume certification/ extension expires at 12 months		Assume certification/ extension expires at 0 months	
Characteristic	**Multivariable HR**	**95% CI**	**Multivariable HR**	**95% CI**	**Multivariable HR**	**95% CI**
Per 3 months increase >12 months	1.04	(1.01 - 1.06)	1.04	(1.02 - 1.06)	1.04	(1.02 - 1.07)
Number of arms, vs. One						
Two	1.33	(1.15 - 1.54)	1.33	(1.15 - 1.54)	1.32	(1.14 - 1.53)
Three or more	1.07	(0.92 - 1.25)	1.07	(0.92 - 1.25)	1.06	(0.91 - 1.24)
Use of randomized allocation†	0.96	(0.83 - 1.12)	0.96	(0.82 - 1.11)	0.96	(0.82 - 1.11)
Masking vs. Open label†						
Single blind	0.96	(0.83 - 1.11)	0.97	(0.84 - 1.11)	0.97	(0.84 - 1.11)
Double blind	0.91	(0.84 - 0.99)	0.91	(0.84 - 0.99)	0.91	(0.83 - 0.99)
Result reporting requirement in effect	2.77	(2.47 - 3.10)	3.47	(3.03 - 3.97)	180	(45.0 - 716)

These analyses assume that certifications or extension requests expire at 18, 12, or 0 months after the date the certification is first received, respectively.
*Enrollment from registration data.
†Single-arm studies assigned a value of “no” for randomization. Non-randomized studies assigned a value of “open” for blinding.

Table S14. Results Reporting over Time among Trials Required to Report, Stratified by Funding Source

Trial is counted in denominator as required to report if time is ≥13 months from primary completion date and ≥24 months beyond certification or extension request date.

	All trials (N=13,327)	**Industry (N=8736)**	**NIH (N=1899)**	**Other (N=2692)**	**NIH+Other (N=4591)**
Months after primary completion date, n/N (%)*					
13 months	1772/11223 (15.8)	1466/6721 (21.8)	152/1845 (8.2)	154/2657 (5.8)	306/4502 (6.8)
24 months	3224/11248 (29.6)	2404/6745 (36.7)	378/1846 (21.2)	442/2657 (17.5)	820/4503 (19.0)
36 months	4184/11833 (38.9)	3002/7313 (44.6)	555/1860 (32.9)	627/2660 (27.1)	1182/4520 (29.6)
48 months	4818/12822 (44.3)	3429/8256 (48.1)	676/1885 (43.0)	713/2681 (33.1)	1389/4566 (37.5)
60 months	5056/13063 (48.9)	3580/8483 (51.8)	734/1892 (51.3)	742/2688 (36.8)	1476/4580 (43.4)

* n= number of trials with results, N = number of trials required to report, % = KM estimate of reporting rate.

Manual Review for False-Positive and False-Negative Findings

To estimate rates of false-positive and false-negative findings, we also conducted a manual review of a random sample of 205 HLACTs (135 industry-funded trials and 35 each from NIH and academia/other-government funding sources) from the trials included in our analysis, and a targeted sample of 100 non-HLACTs drawn from 3711 trials excluded from our analysis based on the National Library of Medicine (NLM)-based algorithm. This targeted group of non-HLACTs was predicted by NLM leaders to be at high risk for being missed by the algorithm because interventions are often incorrectly listed (personal communication, Dr. Zarin, 10/10/2014). HLACTs were sampled from those trials for which intervention type was not listed as biologics, drugs, devices, genetics, or radiation. Determinations made during manual review were based on a trial's use of an FDA-regulated medical product. We also determined whether the HLACT was required to report based upon the approval date for the medical product or indication, as well as the HLACT primary completion date.

Detailed results of these analyses are displayed in Tables S15A and S15B below.

Table S15A. Estimated Proportion of False Positives by Funding Source
Random sample of trials selected from among HLACTs included in analysis, stratified by funding source.

	Industry (N=135)	NIH (N=35)	Other (N=35)
False positive determination (strict definition of ACT and reporting requirements), n (%)			
Not HLACT	0 (0.0)	3 (8.6)	6 (17.1)
HLACT - results not required	64 (47.4)	2 (5.7)	3 (8.6)
HLACT - results required	71 (52.6)	30 (85.7)	26 (74.3)
False positive determination (liberal definition of ACT and reporting requirements), n (%)			
Not HLACT	0 (0.0)	2 (5.7)	2 (5.7)
HLACT - results not required	59 (43.7)	2 (5.7)	3 (8.6)
HLACT - results required	76 (56.3)	31 (88.6)	30 (85.7)
Manual review of reporting requirements, n/N (%)			
Results not required (Not approved)	57/135 (42.2)	2/33 (6.1)	3/33 (9.1)
Results not required (Unlabeled)	2/135 (1.5)	0/33 (0.0)	0/33 (0.0)
Results required (Approved)	59/135 (43.7)	18/33 (54.5)	20/33 (60.6)
Results required (Unlabeled)	12/135 (8.9)	13/33 (39.4)	9/33 (27.3)
Don't know	5/135 (3.7)	0/33 (0.0)	1/33 (3.0)
Reported results or reason for not reporting (strict), n/N (%)	110/135 (81.5)	16/32 (50.0)	13/29 (44.8)
Reported results or reason for not reporting (liberal), n/N (%)	106/135 (78.5)	16/33 (48.5)	14/33 (42.4)
Results received*			
Overall, n/N (%)	54/135 (40.0)	15/35 (42.9)	11/35 (31.4)
Among HLACTs not requiring results (strict), n/N (%)	8/64 (12.5)	0/2 (0.0)	0/3 (0.0)
Among HLACTs requiring results (strict), n/N (%)	46/71 (64.8)	14/30 (46.7)	10/26 (38.5)
Among HLACTs not requiring results (liberal), n/N (%)	7/59 (11.9)	0/2 (0.0)	0/3 (0.0)
Among HLACTs requiring results (liberal), n/N (%)	47/76 (61.8)	14/31 (45.2)	11/30 (36.7)
Certification or extension request received†			
Overall, n/N (%)	32/135 (23.7)	1/35 (2.9)	0/35 (0.0)
Among HLACTs not requiring results (strict), n/N (%)	26/64 (40.6)	1/2 (50.0)	0/3 (0.0)
Among HLACTs requiring results (strict), n/N (%)	6/71 (8.5)	0/30 (0.0)	0/26 (0.0)
Among HLACTs not requiring results (liberal), n/N (%)	23/59 (39.0)	1/2 (50.0)	0/3 (0.0)
Among HLACTs requiring results (liberal), n/N (%)	9/76 (11.8)	0/31 (0.0)	0/30 (0.0)

*Results first received by ClinicalTrials.gov at any time through September 27, 2013.
†Certification or extension request received by ClinicalTrials.gov at any time through September 27, 2013.

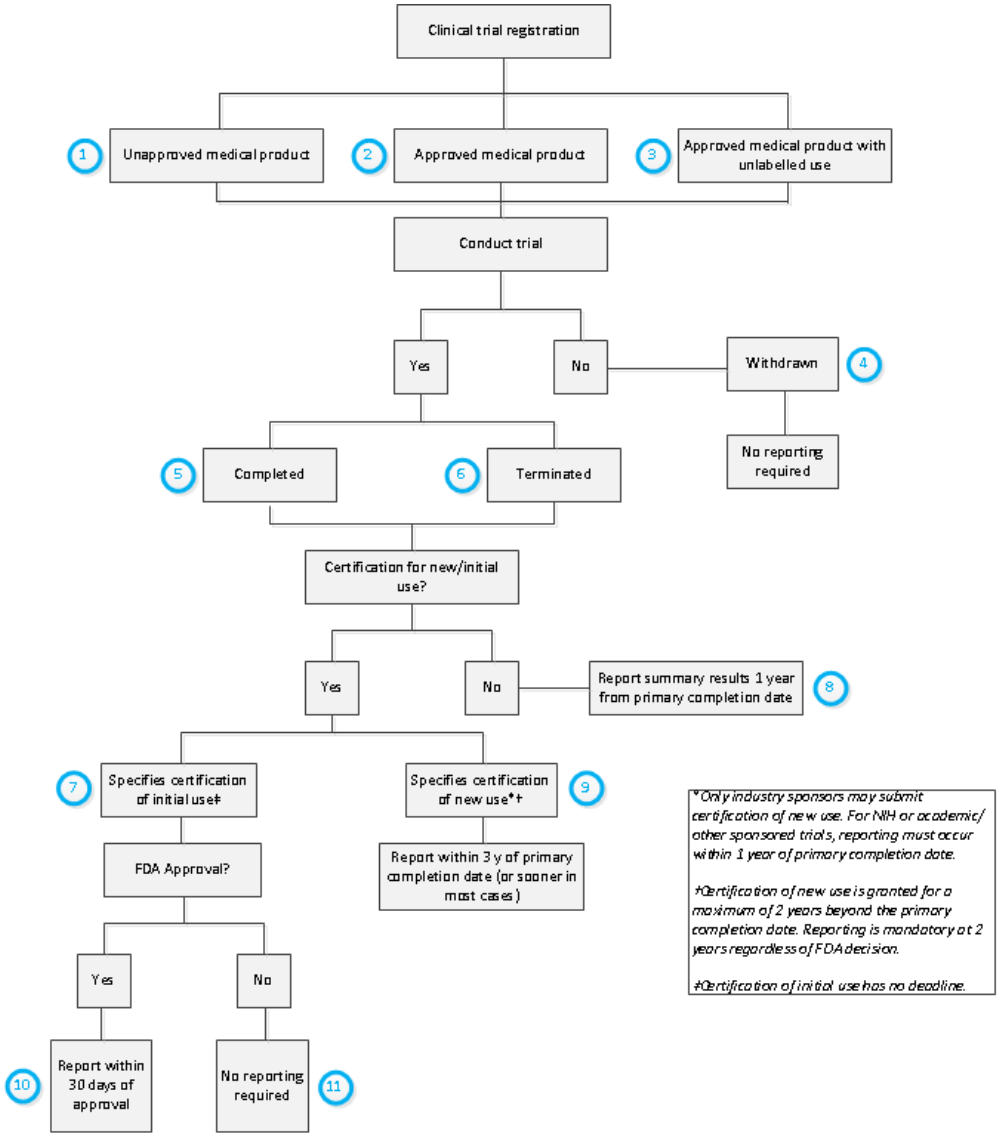
Table S15B. Estimated Proportion of False Negatives in Targeted Subset of Trials not Counted as HLACTs by Intervention Type

*Sample of n=100 trials selected from trials that meet all criteria for being a HLACT except that they do not indicate studying a drug, biological, device, genetic, or radiation intervention.**

	All (N=100)	Behavioral (n=50)	Procedure (n=19)	Dietary supplement (n=7)	Other intervention (n=36)
HLACT - low estimate, n (%)	16 (16.0)	1 (2.0)	5 (26.3)	4 (57.1)	7 (19.4)
HLACT - high estimate, n (%)	19 (19.0)	2 (4.0)	7 (36.8)	4 (57.1)	7 (19.4)
Intervention types*, n (%)					
Behavioral	50 (50.0)	–	–	–	–
Procedure	19 (19.0)	–	–	–	–
Dietary supplement	7 (7.0)	–	–	–	–
Other intervention	36 (36.0)	–	–	–	–

*Study may have more than one intervention type and be counted in >1 row and >1 column.
HLACT, highly likely applicable clinical trial

Figure S4. Reporting Requirements for Medical Products Based and Trial Completion Status



1. Products not approved for any indication at the time of trial initiation are not required to report summary results if they either do not seek approval or if approval is denied. This creates ambiguity, because the requirement for results reporting is not known until an approval occurs, which can be months to years after trial completion. The primary ethical concern is that toxicities of products that are denied approval may never be known, potentially producing risk for patients enrolled in trials of similar products by unwitting investigators and sponsors.
2. Trials involving approved medical products including drugs, devices, biologics, generic products, and radiological products must report results for on-label use within 1 year of trial completion (see #5). Nutritional supplements or food products used to modify disease processes are considered drugs and are required to report if there is a health claim. For these types of products, the intent of the trial is often unclear from the initial registration.
3. Trials of an off-label use of approved products must be reported by 1-year post trial completion for trials not sponsored by manufacturers. Industry-sponsored trials for which the sponsor plans to seek marketing of a new labeled indication can file a Certification of New Use; if certification is granted by the FDA, the sponsor is granted an additional 2 years before mandatory reporting.
4. A clinical trial registration can be withdrawn if no subjects/participants have been enrolled, regardless of the type of intervention because there are no results to report.
5. Trials are considered complete when the last enrolled patient was examined or received an intervention for the purposes of final collection of data for the primary outcome, whether the clinical trial concluded according to the pre-specified protocol or was terminated. There is uncertainty about when the completion date occurs for terminated trials, despite the definition. There are many circumstances in which the final date for data collection is ambiguous, especially when there are multiple co-primary endpoints, or when the trial continues beyond the primary endpoint to collect additional longer-term information.
6. Trials terminated before planned completion may not have complete data collection and the required reporting date is not well-defined. This is concerning because the detailed outcomes may be critical to understanding the toxicity of a product if the trial is stopped early for adverse outcomes.
7. A Certification of Initial Use can be filed by industry seeking a new approval of a previously unapproved product. This certification is determined by the FDA and the required results reporting is within 30 days after approval. However, if the product is not approved, results reporting is not required at any time.
8. Unless there is a special circumstance (see #5, #8, and #10), results reporting is required within 1 year of the primary completion date.
9. When an industry manufacturer plans to seek a new label for a product that is already approved for a different indication, it can file for certification for off-label approved products. This provides a 2-year delay from trial completion until the requirement for results reporting.
10. Results reporting is required when the product or indication is approved. When FDA approves a medical product for marketing, reporting is mandatory within 30 days beyond the approval date.
11. Trials testing unapproved medical products, for which the FDA denies approval or the IND/IDE is withdrawn, are never required to report results to ClinicalTrials.gov.